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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/813,093	03/19/2001	Terry Allen Hauser	2000.688USPD	1404

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EXAMINER
MAYES, LAURIE A

ART UNIT	PAPER NUMBER
1653	9

DATE MAILED: 07/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/813,093	HAUSER ET AL.	
	Examiner	Art Unit	
	Laurie Mayes	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Specification

The use of the trademark AMBERCHROM (p. 13, line 35, p. 14, line 8, p. 15, lines 7-8, 19, 22, 25, 26, 32 and 35, p. 16, lines 2, 20, 27 and 35 and p. 17, line 12), has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 9, 10, 14 and 17-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claims 9, 10, 14 and 17-22, the language "between about . . . and about" is indefinite as it is unclear which term controls the bounds of the claims. The term "about" means a range above and below each of two named limits while "between" means within the two limits. Suggested language is "from about x to about y" for claims 9, 10, 14 and 17-19 and "between x to about y" for claims 20 and 21. Further, in claims 20 and 21, could the amount of hexane be less than 0%? In claim 22, it is unclear as to what would have been the "further purification" of the molecule.

Claim 5 recites the limitation "claim 5". There is insufficient antecedent basis for this limitation in the claim. While it appears to be a typographical error, it is unclear as to which of claims 1, 2, 3 or 4 claim 5 depends from.

Claims 14, 20 and 21 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth above and to include all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6, 9, 10 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frye et al. (US 6,008,041) in view of Mauer et al. and in further view of Varkey et al. Frye et al. teach a method for purifying a human growth hormone (hGH)(present claims 1-4, 16) by

reverse phase liquid chromatography (col. 38, lines 52-58)(present claim 1) wherein the column has a diameter of 30 cm (col. 35, lines 35-40, Ex. 7)(present claims 9 and 10). Frye et al. do not teach a method where the column is filled with a diol.

Maurer et al. (US 5,801,039) teach that adding a diol to an aqueous mixture stabilizes protein in the mixture (col. 13, line 46 and col. 14, lines 10-11) (present claim 1).

Varkey et al. (J. Peptide Res. 51, 49-54 (1998)) teach that a 1,6 hexanediol resin (p. 49, col. 2, 1st para.)(present claim 1, 6) lends to mechanically stablility (p. 51, col. 1, 3rd para.) in an aqueous mixture containing peptides (p. 50, entire page) and has good solvation properties (col. 51, para. 4)(present claims 1, 6).

Given the advantages as taught by Maurer et al. of adding a diol to aqueous solution and that 1, 6 hexanediol lends stability to a resin as taught by Varkey et al., it would have been obvious to one of ordinary skill in the art at the time of the invention by the applicant to use 1, 6 hexanediol to stabilize the aqueous solution in Frye et al.'s method for purifying a human growth hormone (hGH) by reverse phase chromatography (col. 38m lines 52-58) wherein the column has a diameter of 30 cm (col. 35, lines 35-40, Ex. 7) and to repeat the process if further purification is desired (present claims 1 and 22). Thus, the claimed invention was prima facie obvious to make and use at the time the claimed invention was made.

Claims 1-4, 7, 11, 12, 13 and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowman et al. (US 5,994,511) in view of Mauer et al. and in further view of Varkey et al. Lowman et al. teach a method of purifying human growth hormone (hGH) (col. 28, lines 38-43)(present claims 1-4, 16) by high performance reverse phase liquid chromatography (col. 52, lines 38-40)(present claims 1, 7) and wherein the column contains the

polymeric resin styrene divinylbenzene as the styrenic resin allow for faster flow rates and shorter processing times than with other matrices (col. 52, lines 31-36)(present claims 11, 12) and methacrylate gels as a suitable matrix (col. 27, lines 20-21)(present claim 13) and wherein the buffer is determined based on the compositions involved, as buffering agents help to maintain the pH in the range which approximates physiological conditions, and has a pH 8 for certain proteins (col. 82, lines 41-48)(present claims 17-19). Lowman et al. do not teach a method for purifying proteins wherein the buffer contains 1,5 pentanediol, 1, 6 hexanediol or 1,7 heptanediol.

Given the advantages as taught by Maurer et al. of adding a diol to aqueous solution and that 1, 6 hexanediol lends stability to a resin as taught by Varkey et al., it would have been obvious to one of ordinary skill in the art at the time of the invention by the applicant to use 1, 6 hexanediol to stabilize the aqueous solution in Lowman et al.'s method for purifying a human growth hormone (hGH) by high performance reverse phase chromatography. Thus, the claimed invention was prima facie obvious to make and use at the time the claimed invention was made.

Claims 1-4 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayenga et al. (US 6,437,101) in view of Mauer et al. and in further view of Varkey. Hayenga et al. teach a method of purifying human growth hormone and growth hormone antagonist (present claim 15) comprising reverse phase high performance liquid chromatography (col. 10, lines 30-36)(present claims 1-4). Hayenga et al. do not teach a method where the column is filled with a diol.

Maurer et al. (US 5,801,039) teach that adding a diol to an aqueous mixture stabilizes protein in the mixture (col. 13, line 46 and col. 14, lines 10-11).

Varkey et al. (J. Peptide Res. 51, 49-54 (1998)) teach that a 1,6 hexanediol resin (p. 49, col. 2, 1st para.) lends to mechanically stablility (p. 51, col. 1, 3rd para.) in an aqueous mixture containing peptides (p. 50, entire page) and has good solvation properties (col. 51, para. 4).

Given the advantages as taught by Maurer et al. of adding a diol to aqueous solution and that 1, 6 hexanediol lends stability to a resin as taught by Varkey et al., it would have been obvious to one of ordinary skill in the art at the time of the invention by the applicant to use 1, 6 hexanediol to stabilize the aqueous solution in Frye et al.'s method for purifying a human growth hormone (hGH) by reverse phase chromatography (col. 38m lines 52-58) wherein the column has a diameter of 30 cm (col. 35, lines 35-40, Ex. 7) and to repeat the process if further purification is desired. Thus, the claimed invention was prima facie obvious to make and use at the time the claimed invention was made.

Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frye et al. (US 6,008,041) in view of Mauer et al. and Varkey et al. and in further view of Yu et al. (Journal of Chromatography A, 725 (1996) 149-155). Frye et al. teach a method for purifying a human growth hormone (hGH) by reverse phase liquid chromatography (col. 38, lines 52-58) wherein the column has a diameter of 30 cm (col. 35, lines 35-40, Ex. 7)(present claim 1). Frye et al. do not teach a method where the column is filled with a diol or wherein the column is a preparative column.

Maurer et al. (US 5,801,039) teach that adding a diol to an aqueous mixture stabilizes protein in the mixture (col. 13, line 46 and col. 14, lines 10-11)(present claim 8).

Varkey et al. (J. Peptide Res. 51, 49-54 (1998)) teach that a 1,6 hexanediol resin (p. 49, col. 2, 1st para.) lends to mechanically stablility (p. 51, col. 1, 3rd para.) in an aqueous mixture containing peptides (p. 50, entire page) and has good solvation properties (col. 51, para. 4).

Yu et al. teach a method of separating proteins from analytes and comprising loading the mixture onto a reverse phase liquid chromatography column prepared with alkyl-diol silica (ADS) (see abstract). While Yu et al. does teach an alkyl-diol (alkyl-diol silica or ADS) loaded onto a preparative column and wherein the buffer is at a pH of 7.4 (p. 150, col. 2, 2nd para.), Yu et al. do not teach a method wherein the buffer comprises 1,5 pentanediol, 1,6 hexanediol or 1,7 heptanediol.

Given the advantages as taught by Maurer et al. of adding a diol to aqueous solution and that 1, 6 hexanediol lends stability to a resin as taught by Varkey et al., it would have been obvious to one of ordinary skill in the art at the time of the invention by the applicant to use 1, 6 hexanediol to stabilize the aqueous solution in Frye et al.'s method for purifying a human growth hormone (hGH) by reverse phase chromatography (col. 38m lines 52-58) wherein the column is a preparative column as taught by Yu et al. and has a diameter of 30 cm (col. 35, lines 35-40, Ex. 7). Thus, the claimed invention was prima facie obvious to make and use at the time the claimed invention was made.

Claims 1, 2, 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frye et al. (US 6,008,041) in view of Mauer et al. and Varkey et al. and in further view of Kahne et al. (US 5,693,769). Frye et al. teach a method for purifying a human growth hormone (hGH) by reverse phase liquid chromatography (col. 38, lines 52-58) wherein the column has a diameter of

30 cm (col. 35, lines 35-40, Ex. 7)(present claims 1, 2, 4). Frye et al. do not teach a method where the column is filled with a diol.

Maurer et al. (US 5,801,039) teach that adding a diol to an aqueous mixture stabilizes protein in the mixture (col. 13, line 46 and col. 14, lines 10-11)(present claims 1, 2, 4).

Varkey et al. (J. Peptide Res. 51, 49-54 (1998)) teach that a 1,6 hexanediol resin (p. 49, col. 2, 1st para.) lends to mechanically stablility (p. 51, col. 1, 3rd para.) in an aqueous mixture containing peptides (p. 50, entire page) and has good solvation properties (col. 51, para. 4)(present claims 1, 2, 4).

Kahne et al. teach a method of purifying enkephalin by reverse phase liquid chromatography (col. 36, lines 30-40)(present claim 5). Kahne et al. do not teach a method wherein the buffer contains 1,5 pentanediol, 1, 6 hexanediol or 1,7 heptanediol.

Given the advantages as taught by Maurer et al. of adding a diol to aqueous solution and that 1, 6 hexanediol lends stability to a resin as taught by Varkey et al., it would have been obvious to one of ordinary skill in the art at the time of the invention by the applicant to use 1, 6 hexanediol to stabilize the aqueous solution in Frye et al.'s method for purifying a protein by reverse phase chromatography (col. 38m lines 52-58) wherein the protein to be purified is enkephalin. Thus, the claimed invention was prima facie obvious to make and use at the time the claimed invention was made.

Conclusion

Claims 1-22 are rejected. Arakawa et al (Arch. Biochem. Biophys. 224(1):169-177 (1983)) is cited as disclosure that it is known in the art that diols stabilize protein in aqueous solution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laurie Mayes whose telephone number is (703) 605-1208. The examiner can normally be reached on Monday through Friday from 9 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1123.

L. Mayes

Laurie Mayes
Patent Examiner
Art Unit 1653
July 16, 2003

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